

Access to health services for the control of cancer of the uterine cervix in promary care

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RESEARCH

ACCESS TO HEALTH SERVICES FOR THE CONTROL OF CANCER OF THE UTERINE CERVIX IN PRIMARY CARE
 ACESSO A SERVIÇOS DE SAÚDE PARA O CONTROLE DO CÂNCER DO COLO UTERINO NA ATENÇÃO BÁSICA*
 ACCESO A LOS SERVICIOS DE SALUD PARA LA LUCHA CONTRA EL CÁNCER DE CUELLO UTERINO EN ATENCIÓN PRIMARIA

Magna Maria Pereira da Silva¹, Maria Teresa Cicero Lagana², Clélia Albino Simpson³, Ana Michele de Farias Cabral⁴

ABSTRACT

Objective: To analyze the control of cancer of the cervix from the focus of access to health services. **Method:** A cross-sectional study using consultation documentary and household survey with analysis of calculation of frequencies of selected variables. **Results:** The results of the last cytological examination showed higher frequency of squamous metaplasia immature; intraepithelial lesion of low grade (LSIL); Intraepithelial Lesion high grade (HSIL) and atypical squamous cells of undetermined significance (ASC-US), predominantly in women in the age group 25 to 64, brown, married/marital harmony and housewives, with clinical complaints of vaginal discharge, bleeding and the occurrence of stds (including HPV). **Conclusion:** There is no longitudinal follow-up of women in the geographical area of enrollment 47 of USF Nova Natal II from the collection of cytological examination until the discharge by cure. **Descriptors:** Gynecologic nursing, Malignant neoplasm of the uterine cervix, Follow-up, Access to health services.

RESUMO

Objetivo: Analisar o controle do câncer do colo uterino a partir do enfoque do acesso a serviços de saúde. **Método:** Estudo transversal utilizando-se consulta documental e inquérito domiciliar com análise do cálculo de frequências de variáveis selecionadas. **Resultados:** Os resultados do último exame citológico mostraram maior frequência de metaplasia escamosa imatura; lesão intraepitelial de baixo grau (LSIL); lesão intraepitelial de alto grau (HSIL) e células escamosas atípicas de significado indeterminado (ASC-US), predominantemente em mulheres na faixa etária de 25 a 64, pardas, casadas/convivência marital e donas de casa, com queixas clínicas de corrimento, sangramento e ocorrência de DSTs (inclusive HPV). **Conclusão:** Não há acompanhamento longitudinal das mulheres na área geográfica de adscrição 47 da USF Nova Natal II desde a coleta do exame citológico até a liberação da mulher, pela alta, do programa de controle do câncer de colo uterino. **Descritores:** Enfermagem ginecológica, Neoplasia maligna do colo de útero, Seguimentos, Acesso a serviços de saúde.

RESUMEN

Objetivo: Analizar la lucha contra el cáncer del cuello del útero con el enfoque de acceso a los servicios de salud. **Método:** Estudio transversal mediante consulta documental y una encuesta de hogares con análisis de cálculo de frecuencias de variables seleccionadas. **Resultados:** Los resultados del último examen citológico mostraron una mayor frecuencia de metaplasia escamosa inmadura; lesión intraepitelial de bajo grado (LSIL); lesión escamosa intraepitelial de alto grado (HSIL) y células escamosas atípicas de significado indeterminado (ASC-US), principalmente en las mujeres en el grupo de edad de 25 a 64, de piel morena, casadas/armonía conyugal y amas de casa, con quejas clínicas de la secreción vaginal y sangrado, y la aparición de las ETS (incluyendo el VPH). **Conclusión:** No hay un seguimiento longitudinal de las mujeres en el área geográfica de inscripción 47 de USF Nova Natal II a partir de la colección de examen citológico hasta la liberación de la mujer, por la alta del programa de control de cáncer del cuello uterino. **Descriptores:** Enfermería ginecológica, Neoplasias malignas del cuello uterino, Seguimiento, Acceso a servicios de salud.

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INTRODUCTION

Malignant neoplasm of the cervix is the second most common type of cancer among women worldwide. The northeast ranks second in incidence among Brazilian regions with 17 cases per 100 000 women.¹⁻²

Besides the high incidence, mortality from cervical cancer in Brazil is considered high, between 5 and 6 deaths/100,000 women/year.² Keeping mortality rates too high can be attributed to the low coverage of the Pap test, the discontinuation of prenatal diagnosis of early precursor lesions, the poor quality of Pap smears performed in the country and the limitations of SISCOLO (A database of the cervix cancer) which does not identify women out of the tracing system to bring them to repeat the examinations or run them for the first-time or even provide longitudinal information that records the care over time, preventing the organized tracing of women.³⁻⁶

Confronting the national policies for cervical cancer control with the precariousness of the results has been a major challenge to be overcome by the Brazilian public health, which makes two questions arise.

The first is what separates us from reaching the resolution in the control of malignant neoplasm of the cervix beyond merely programmatic action in Primary Care, by achieving results in the Unified Health System (SUS)?

And the second is: if the control of malignant neoplasm of the cervix in Primary Care is defined as a priority in the national political agenda, why doesn't it succeed in improving indicators of this disease?

Regarding the first question on achieving a resolution in the control of malignant neoplasm of the cervix, it is known that Primary Care must act on health surveillance with the ability to

incorporate a set of professionals and knowledge to perform a multidisciplinary and intersectoral approach, and the Family Health Program (PSF), the critical part of the organization.^{8, 9}

By analyzing the agreed indicators for the early detection of cervix cancer in the National Institute Cancer Informative (INCA), a federal unit, we can observe a low percentage of treatment/follow-up of precursor lesions (intraepithelial neoplasia grades II and III, high grade), in Rio Grande do Norte, during the period from 2009 to 2010. Of a total of 511 cases of high-grade lesions diagnosed, only 6.1% were being followed.¹⁰

This situation illustrates the fragility of health surveillance of women regarding the monitoring of malignant neoplasm of the cervix in the territory.

The intraepithelial neoplasia grades II and III are premalignant changes or malignancies diagnosed in Pap smear considered high grade, since about 75% of patients with this analysis result will show histopathological confirmation and approximately 2% of them have a histopathologic diagnosis of carcinoma attacker. Therefore, all patients with suggestive cytology of high-grade lesion in units of Primary Care should be referred immediately to the Reference of Medium Complexity Unit for colposcopy, as the initial approach, but most women cannot continue the treatment due to restrictions to specialized care, which brings us to the question of solvability.¹¹

Regarding the second question on the definition of control of cervix malignant neoplasm in Primary Care as a priority on the national political agenda, unfortunately, not always the priority setting comes with a political analysis of viability, of a sustainability project or of real interest to confront it. In contrast, studies examining outcome indicators of public policies

have shown that there is an increasing gap between the so called ‘formulation stage’, where they elect health problems and decided to implement the guidelines and policies in general; this is where a project is born.^{12, 13}

The screening for cervical cancer is being executed in Basic Health Units and the fact is that the decentralization of Pap smears performed in these units made the access of women easier to this kind of examination. Prevention of cervical cancer is an activity inherent to family health teams, defined as the Pact for Health Strategy, according to Decree 399/06 of the Ministry of Health and formally assumed by municipal managers.¹⁴

From the point of view of social benefits for women, we question the glaring discrepancy between what is advocated by public policy and what actually happens in practice.

Epidemiological data show a disregard for the rights of sanitation of a large portion of the female population that has in public services the only health care alternative. This is easily seen when we analyze the high mortality of women with a type of cancer that has the highest levels of healing, with possible prevention in almost all primary care services.^{15,16}

Given these projections, cases of illness in relatively advanced stages at the time of diagnosis have contributed to increased number of mortality, also affecting the survival rates of these women. In developed countries the average survival rates, estimated in five years, ranges from 69% to 79%, in Brazil it is 49%.^{1,5}

The control of this disease, includes several actors (states, municipalities, healthcare professionals, educational institutions and users), while, on the other hand there is a scenario of weaknesses, especially in primary care, which does not guarantee the proper treatment and tracking of detected cases of precursor lesions and neoplastic lesions.^{9,10}

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Control of cervical cancer points to the possibility of municipalities carrying out those assignments of primary care, through access to Specialized Care and Hospital Care in surveillance of cases referred for diagnostic and treatment confirmation, promoting a flowchart to take care of women in various levels of the health system in the municipality in guiding treatment of high-grade lesions; in the systematic monitoring of all women with positive cytology and histopathology examination until completion of treatment and case closure.⁶

The aim of this study was to analyze the control of cervical cancer in primary care according to the access to health services through selected variables and home verification, following the situation of women whose cytological test results had changes.

METHODOLOGY

Cross-sectional study to analyze access to health services for women with specific sociodemographic and clinical characteristics who underwent cytological examination and showed modified diagnosis in cervix malignant neoplasm control.

The study was conducted at the Family Health Unit Nova Natal II (New Nova Natal II USF) in the city of Natal/RN where care for the realization of cytological examination is scheduled. In this case, only nurses perform the collection of cytological material. The assistance to women does not always include easy geographical access.

The target population consisted of 1170 women living in the geographical area of area 47 ascription of the Nova Natal II USF, who had undergone cytological exams and were registered in the books of registry ‘Tracking Women's Program’ of the USF SISCOLO of Nova Natal II in the period of January 2005 to August 2010. Of these, we found 54 women diagnosed with

abnormal cytology, which constituted the convenience sample of the study, sixteen of which were not home during the household survey, eleven for changes of address and five being outside the area, resulting in 38 women.

Eligibility criteria of intentional sample were women aged over 18 at the time of research, with any educational level and ethnicity; having changes in the cervical cytology exam; able to answer the questions in the survey form and who had agreed to participate and signed the consent form (ICF).

We excluded women who were not part of enrolled area; who did not show changes in cervical cytology and had changed address during the household survey.

The research technical procedures used were documentation query from secondary sources (the Registry Tracking Women's Program book from USF SISCOLO Nova Natal II-Medical records and family) and the household survey, using the "Form of interview for control of malignant neoplasm of the cervix uteri in Primary Care" based on models used in other studies^{17, 18} and after the pilot test.

We considered independent variables those of sociodemographic characteristics and of clinical diagnosis and dependent variables those of monitoring, explained in Table 1.

Variables		
Independent Variables	sociodemographic variables	Age Group Schooling Ethnicity Married / Living marital Housewife
	Clinical Variables	Sexual Partners Discharge Bleeding STDs (including HPV) Result of last cytologic exam
Dependent Variables	Monitoring variables	Monitoring

Table 1. Table of variables.

The variable ‘result of last preventive exam’ followed the Brazilian Nomenclature for Reporting Cervical and Recommended Conducts¹¹ rules as shown in Table 2.

Cytological Abnormalities	
Benign Amendment	Immature squamous metaplasia.
Premalignant or Malignant Changes	Atypical squamous cells of undetermined significance possibly non-neoplastic.
	Low-grade squamous intraepithelial lesion (including cytopathic effect of HPV and cervical intraepithelial neoplasia grade I).
	High-grade intraepithelial lesions (cervical intraepithelial neoplasia including grade II and III).

Table 2. Benign Amendment and premalignant or malignant changes.

Statistical analysis was performed using the open source software Minitab® 16 and free statistical software R, applying the Chi-square test with significance level of 5%.

The study was approved by the IRB, Federal University of Rio Grande do Norte under Opinion No. 039/2011.

RESULTS AND DISCUSSION

In this study of a total of 1170 women who had a Pap test during the study period, 4.6% (53) were diagnosed with cervical abnormalities, of which sixteen were not found, totaling 38 women to be visited at home and be interviewed. Similar studies on cytological diagnosis of atypical squamous cells found 1.4% of abnormalities¹⁹ and squamous or glandular cells showed rate of 6.4%, compared to average estimates of Brazilian INCA, 4%²⁰.

The results of the last test with cytological diagnosis of cervical abnormalities can be seen in Table 3.

The result of the benign change was immature squamous metaplasia, which was considered since it is characterized as an inflammatory type, vulnerable to HPV infection in young patients due to early exposure of the cervix transformation zone to sexually transmitted agents associated with local conditions as ectopia and inflammatory processes, with possible subsequent evolution to the lower genital tract neoplasia.^{11, 21}

The result of pre-malignant or malignant changes were LSIL, HSIL and the ASC-US.

Sociodemographic and clinical variables	Results from last cytological exam with a diagnosis of cervical abnormalities.			
	Immature Squamous metaplasia	LSIL	HSIL	ASC-US
	(N=38) %	(N=38) %	(N=38) %	(N=38) %
Age group				
18 to 24	02 (9,5)	05 (41,7)	00 (0,0)	00 (0,0)
25 to 64	19 (90,5)	06 (50,0)	03 (100,0)	02 (100,0)
+ 65	00 (0,0)	01 (8,3)	00 (0,0)	00 (0,0)
Ethnicity				
Brownish	13 (61,9)	08 (66,7)	01 (33,3)	01(50,0)
White	06 (28,6)	03 (25,0)	00 (0,0)	00 (0,0)
Black	02 (9,5)	01 (8,3)	02 (66,7)	01(50,0)
Married/ Marital Cohabitation	17 (80,9)	06 (50,0)	01 (33,3)	02 (100,0)
Discharge	10 (47,5)	04 (33,3)	02 (66,7)	00(0,0)
Bleeding	01 (4,8)	00 (0,0)	00 (0,0)	00 (0,0)
DSTs (including HPV)	00 (0,0)	03 (25,0)	01 (50,0)	00 (0,0)

LSIL = low-grade squamous intraepithelial Injury (including cytopathic effect of HPV and cervical intraepithelial neoplasia grade I).
HSIL = Squamous intraepithelial high-grade Injury (including cervical intraepithelial neoplasia grades II and III).
ASC-US = Atypical squamous cells of undetermined significance; possibly non-neoplastic.

Table 3. Last exam results with cytologic diagnosis of cervical abnormalities according to sociodemographic and clinical variables.

The cervical immature squamous metaplasia amendment, was predominant in women aged 25 to 64 years old (90.5%) of mixed ethnicity (61.9%), married or living together in marital status (80.9%), discharge (47.6%) and (4.6%) bleeding.

The LSIL was predominant in women aged 25 to 64 years old (50.0%) of mixed ethnicity (66.7%), married or living together in marital status (50.0%), with discharge (33.3%) and (25%) of STDs (including HPV).

The HSIL was also predominant in women aged 25 to 64 years old(100.0%), black ethnicity

(66.7%) and brown (33.3%), married or living together in marital status (only 01 - 33.3%), with discharge (66.7%) and (50.0%) of STDs (including HPV).

Finally, the ASC-US were predominant in women aged 18 to 24 years old (100%) in women of mixed ethnicity (50%) and black (50%), married or living together in marital status (100%).

Table 4 shows possible associations of the data of the women according to sociodemographic and clinical variables.

Sociodemographic and clinical variables	Follow-up Completion		
	No	Yes	Value -p
	(N=38) %	(N=38) %	
Age Group			
18 to 24	04 (57,1)	03 (42,9)	1,000
25 to 64	16 (53,3)	14 (46,7)	
Above 65	01 (100,0)	00 (0,0)	
Ethnicity			
brown	13 (56,5)	10 (43,5)	0,685
white	04 (44,4)	05 (55,6)	
black	04 (66,7)	02 (33,3)	
Education *			
Until elementary school	12 (54,5)	10 (45,5)	
High School	09 (64,3)	05 (35,7)	
Higher Education	00 (0,0)	01 (100,0)	0.3938
Uneducated	00 (0,0)	01 (100,0)	
Housewife			
No	06 (50,0)	06 (50,0)	0,658
Yes	15 (57,7)	11 (42,3)	
Married / Living Together			
No	06 (50,0)	06 (50,0)	0,658
Yes	15 (57,7)	11 (42,3)	
STDs (including HPV)			
No	20 (62,5)	12 (37,5)	0,151
Yes	01 (25,0)	03 (75,0)	
Sexual Partners			
One	11 (78,6)	03 (21,4)	0,127
Two	06 (50,0)	06 (50,0)	
Three	02 (28,6)	05 (71,4)	
Over five	02 (40,0)	03 (60,0)	

Table 4. Follow-up Completion of the women according to selected variables.

The analysis of the frequency of selected variables with the completion of follow-up was not statistically significant. The limited sample size may have influenced the results of the dependent

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tests between the variables and other possible associations.

Studies on the prevalence of cervical abnormalities that affect the control of cervical cancer related this finding to the precocity and sexual promiscuity; illiteracy, poor sanitation and the inverse of the number of years at school.²⁰

Given the multiple factors that affect the control of cervical cancer, housewives without their own income are a group that is less likely to adhere to follow-up due to the difficulty of attending repeated consultations, since they have competing activities such as housework or child care.²²

Women with sexually transmitted diseases that present discharge are particularly at risk for cervical cancer, especially among those economically disadvantaged, such as women's area 47 of the Nova Natal II USF. HPV infection rates are high in these groups, associated mainly to the difficulty of access to health services.

Regarding the bleeding variable, carcinoma of the cervix is usually asymptomatic in the initial forms and pre-invasive. However in the advanced disease the most common clinical manifestations are irregular vaginal bleeding or blood loss to intercourse. The presence of bleeding is therefore particularly important in cytology results with high-grade lesions.

The treatment for LSIL, more common in young women, is controversial, since most of them will resolve spontaneously and result in a significant number of unnecessary diagnostic and therapeutic procedures, it is recommended to repeat cytology in 6 months, when then colposcopy is indicated if changes persist. Furthermore, reducing the interventions in cervical cancer in young women is justified in view of epidemiological evidence of increased obstetric and neonatal morbidity in this group and the fact that they do not have offspring set.^{6, 23, 24}

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On the other hand, in older women, the LSIL discloses an unsatisfying colposcopy result and biopsy does not ensure the lack of high-grade lesion, which may be located in the endocervical canal. Given the higher prevalence of pre-invasive lesions and invasive in older women, follow-up smears and colposcopy provides more security to the extent that keeps women under the health service control.²⁵

However, in HSIL, referral for colposcopy should be immediate, the need for treatment by Surgery of High Frequency (SHF), whereas, from the point of view of the patient, the consequences of such treatment are discomforts, stress and potential complications as stenosis and cervical incompetence.^{11, 26}

The result of ASC-US is controversial among pathologists, since it is a report that generates subjectivity. Consequently, the views are quite diverse in relation to the monitoring of patients with this diagnosis. Prevalence studies of cytological diagnosis of atypical squamous cells of undetermined significance, with follow-up examinations every six months by cytology, showed increased risk for the development of cervical cancer and precursor lesions.^{27, 28}

The results presented on the changes of the last cervical screening test performed by the women of the area 47 of the Nova Natal II USF show the need for follow-up including cytological journals, subsequent evaluations in cases of persistent changes, diagnosis and colposcopic directed biopsy and as treatment for CAF colpocytological changes according to conduits standardized by the Ministry of Health.

Therefore, control of cervical cancer is complex because it requires, in addition to collecting specimen for cervical cytology, multiple appointments periodically, control of sexually transmitted diseases; access to diagnosis of the etiologic agent of HPV; appropriate follow-up for changed exams; agile and easy access to services;

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flexibility to schedule and reschedule appointments and fast service.^{5, 29, 30}

Because cervical cancer is the second most common cancer among women worldwide, the disease burden is high in developing countries, where 80% of cases occur. While in developed countries, cervical cancer accounts for 7% of all female malignancies, as in developing countries accounts for 24%. This disparity is attributed to poor tracking and inappropriate monitoring of women with abnormal results, due to the difficulties of access to services and technologies, leading to premature death and years of life lived with physical and psychological sequelae.^{31, 32}

The analysis of women's situation in the area 47 of Nova Natal II USF compared to the control of cervical cancer revealed vulnerabilities for the development of precursor lesions and neoplastic lesions by sociodemographic characteristics related to age, ethnicity, education, marital status and occupation and the clinical diagnosis concerning STDs, the discharge, the bleeding, the number of sexual partners and with benign and pre-malignant cervical cytological changes, since they could not continue to the recommended follow-up, especially due to the difficult access.

Therefore, the resolution in the control showed limitations in relation to the organization of the SUS, which did not provide easy access to disease control actions that go beyond basic care, for appropriate follow-up of women analyzed, with varying degrees of cervical abnormalities, should only be completed with the cure, established with consecutive negative cytological, colposcopic controls and surgical diagnosis and treatment.

In Table 4 it can be seen that the majority of women (21/38) did not follow up because they cannot overcome the difficulties of access to the medium and high complexity reference observed in reports such as "It's hard to schedule surgery," "I J. res.: fundam. care. online 2013. jul./set. 5(3)273-282

did all the tests for the surgery, but I managed to do only after 2 years ", "I could not schedule the colposcopy", "there's no vacancy in the PS to do colposcopy", "It took me a long time to schedule the colposcopy", " I had no SUS card and could not schedule in the central", " It took a lot to schedule the biopsy through SUS which worsened the disease", "I did just the colposcopy, but I could not go to the doctor because they were on strike", " There was no material in the PS to repeat the exam", "I started working and I had no more time "or even," I could not repeat the preventive in the PS ".

IMPLICATIONS

For at least ten years, ideological movements in the public health field as 'Health Promotion', 'Healthy Cities' and Health Surveillance' have pointed to the need for health professionals to focus more on positive health design and practice, since health policies aim at healing the diseases and the preventive dimension of the risks seem to find limits on the ethical reflection of the social benefit that should provide the people.³²

However, today we face significant barriers to entry and reach a resolution in the control of cervical cancer in primary care, even with low-cost effective technologies. There is no guarantee of universal access to the follow-up of women with cervical abnormalities from simpler technologies to more complexes, as we observed in this study. Since women's access to health services is uneven, we reaffirm the importance of the teams of the Family Health Strategy in controlling health of the territory under its responsibility.

The lack of guaranteed access to the resolution of changed cytology of women from area 47 of the Nova Natal II USF, through appropriate treatment, pointed us towards ethical dilemmas facing the conflict on the situation of follow up of women and commitment to make

decisions that promote high quality of care from the point of view of non-maleficence, beneficence and justice.

The Pap test does not provide results immediately, but following workup, a fact that is especially problematic for the female population of the area 47 of Nova Natal II USF, admittedly poor. It requires planning in subsequent schedules. Unfortunately, even with the reorganization of primary care, from the Family Health Strategy, it is yet provided an opportunistic nursing care, ie, the treatment to women has been done with no systematic planning of actions that may promote a longitudinal following up from collection of cytological examination until the liberation of women, through the Program of Cervical Cancer Control.

LIMITATIONS

The analysis occurred starting from secondary data, collected retrospectively, and therefore was restricted to sociodemographic and clinical variables available in the consulted documents.

So the quality of information from family medical records was a limitation. In them, this information was missing or poorly recorded, ie, discharge records, diagnoses of STDs, smoking, Pap test results with cervical abnormalities, first sexual intercourse, number of partners, use and duration of use of oral contraceptives, were not always available in records. We could not find any information on the situation of women who received follow-up results with cervical abnormalities.

As a consequence, during the interviews face to face, the records were subject only to the answers provided by women, a situation that is subject to memory, especially those with less schooling, implying also the information issue.

Another encountered limitation was the difficulty in locating the addresses of women

previously selected due to the rotation of families in the area.

CONCLUSION

The amendment cervical immature squamous metaplasia, was predominant in women aged 25 to 64 years (90.5%) of mixed ethnicity (61.9%), married or living together in marital status (80.9%), with discharge (47.6%) and (4.6%) bleeding.

The LSIL was predominant in women aged 25 to 64 years (50.0%) of mixed ethnicity (66.7%), married or living together in marital status (50.0%), with discharge (33.3%) and (25%) of STDs (including HPV).

The HSIL was also predominant in women aged 25 to 64 years (100.0%), black ethnicity (66.7%), married or living together in marital status (only 01 33.3%) with discharge (66.7 %) and (50.0%) of STDs (including HPV).

Finally, the ASC-US were predominantly aged 18 to 24 years (100%) in women of mixed ethnicity (50%) and black (50%), married or living together in marital status (100%).

The analysis of the frequency of selected variables with the completion of follow-up was not statistically significant.

These results indicate that area 47 of Nova Natal II USF has limitations to meet their demand for women and to refer those cases that require a more specialized care within the health system.

The control of cervical cancer implies the acceptance of women ranging from initial consultation on the unit until the solution of the problem in other levels of care, by providing all the technology available to get the diagnosis and treatment appropriate to each case, which is not happening at area 47 of Nova Natal II USF, since women verbalized difficulties accessing services outside of primary care, to continue the follow-up.

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As a consequence, late diagnosis of the disease can be a public health problem in that area enrolled. Late diagnosis is related to the difficulty of access of women to health services and barriers that hinder solving the management and appropriate referral of suspected cases to research at other levels of the system.

Thus the actions developed in the control of cervical cancer in the area 47 of Nova Natal II has not been sufficient to improve the outcomes of health care for women, because it is also necessary to have complementary actions in higher levels of system.

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